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Title: Universal *BRCA1/BRCA2* testing for ovarian cancer patients is welcomed, but with care: how women and staff contextualize experiences of expanded access

Running head: Universal genetic testing: experiences in ovarian cancer

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Abstract

Decreasing costs of genetic testing and advances in treatment for women with cancer with germline *BRCA1/BRCA2* mutations have heralded more inclusive genetic testing programs. The Genetic Testing in Epithelial Ovarian Cancer (GTEOC) Study, investigates the feasibility and acceptability of offering genetic testing to all women recently diagnosed with epithelial ovarian cancer (universal genetic testing or UGT). Study participants and staff were interviewed to: (i) assess the impact of UGT (ii) integrate patients' and staff perspectives in the development of new UGT programs. Semi-structured interviews were conducted with twelve GTEOC Study participants and five members of staff involved in recruiting them. The transcripts were transcribed *verbatim* and analyzed using Interpretative Phenomenological Analysis. There are two super-ordinate themes: *motivations and influences around offers of genetic testing* and *impacts of genetic testing in ovarian cancer patients.* A major finding is that genetic testing is contextualized within the broader experiences of the women; the impact of UGT was minimized in comparison with the ovarian cancer diagnosis. Women who consent to UGT are motivated by altruism and by their relatives' influence, whilst those who decline are often considered overwhelmed or fearful. Those without a genetic mutation are usually reassured by this result, whilst those with a genetic mutation must negotiate new uncertainties and responsibilities towards their families. Our findings suggest that UGT in this context is generally acceptable to women. However, the period shortly after diagnosis is a sensitive time and some women are emotionally overburdened. UGT is considered a 'family affair' and staff must acknowledge this.

Keywords: UK; BRCA1; BRCA2; Genetic counseling; Interpretive phenomenological analysis (IPA); Ovarian cancer; Oncology

Background

Approximately 1.5% of women in the UK are diagnosed with epithelial ovarian cancer (EOC), and the five-year prognosis remains poor. Up to 15.5% of these women have a germline mutation in their *BRCA1/BRCA2* genes (Zhang et al. 2011). Estimates indicate that limitations of established genetic testing pathways via Clinical Genetics Services mean that only 60% of those with a germline *BRCA1/BRCA2* gene mutation are identified (Metcalfe et al. 2009). There is evidence that *BRCA1/BRCA2* mutation status provides predictive information regarding likelihood of response to treatment, specifically to poly (ADP-ribose) polymerase (PARP) inhibitors (Gelmon et al. 2011; Ledermann et al. 2012, 2014). Indeed, Olaparib (*Lynparza)* has recently been approved by the National Institute for Health and Care Excellence for treating eligible patients with relapsed, platinum sensitive cancer with *BRCA1/BRCA2* mutations (National Institute for Health and Care Excellence 2016).

Identifying more mutation carriers will increase the number of families where cascade genetic testing can be offered, thus increasing identification of female relatives at high risk of EOC and breast cancer. Undertaking bilateral salpingo-oophorectomy in these women reduces the risk of EOC by 80–96% (Domchek et al. 2010; Kauff et al. 2008; Rebbeck et al. 2009); furthermore, risk-reducing bilateral mastectomies significantly reduces the risk of a first diagnosis of breast cancer (Domchek et al. 2010). Despite the benefits of *BRCA1/BRCA2* testing, concerns have been raised about testing too soon after (breast cancer) diagnosis, arguing that it may overburden women already weighed down with their cancer diagnoses (Ardern-Jones et al. 2005). As genetic testing becomes increasingly integrated into mainstream medical practice, it is important that this is undertaken appropriately at the optimum time in the patient diagnostic pathway. In this paper, we draw on the experiences of those involved in an early implementation study modeling how

expanded access to genetic testing could be achieved in practice: The Genetic Testing in Epithelial Ovarian Cancer (GTEOC) Study. The quantitative arm of the GTEOC Study, concerned with genetic testing strategy, mutation identification rate, cost consequences analysis, and quantitative analyses of psychological impact and acceptability is reported elsewhere (Plaskocinska et al. 2016). Qualitative work is vital at this initial stage to enable the development of effective training for staff involved in these new clinical pathways. Few previous studies have explored timing of diagnostic genetic testing. Regarding the GTEOC study, we use the term 'universal genetic testing' (UGT) as this best fits the purpose and strategy. In the literature reviewed, there is reference to 'rapid genetic testing' (RGT) or 'treatment focused genetic testing' (TFGT); for clarity, we will use the term RGT when referring to previous research. Though there are commonalities (i.e. testing relatively soon after diagnosis), we differentiate between these terms and UGT as the other terms do not capture the element of broadening access to genetic testing.

Previous qualitative research has suggested that the influence of RGT on treatment decisions for EOC overrides other psychosocial concerns (Gleeson et al. 2013; Meiser et al. 2012). A recent qualitative study involving both breast and ovarian cancer patients describes women's preferences for personalized professional involvement to enable decision making (Augestad et al. 2017). However, this study took place when the results of genetic testing did not influence treatment decisions and only one of the seventeen participants had a *BRCA1/BRCA2* mutation. Younger women diagnosed with breast cancer generally have positive attitudes towards RGT (Zilliacus et al. 2012), though the focus on immediate treatment decisions may mean considering further implications of the testing is delayed.

Quantitative work evaluating RGT in the context of breast cancer diagnosis (Schlich-Bakker et al. 2006, 2008; 2009) indicates that there is no impact on short- or long-term psychological distress of being approached about genetic testing, though in one study 43% of eligible patients declined counseling and/or genetic testing (Schlich-Bakker et al. 2008) highlighting potentially important acceptability issues. Similarly, no adverse psychosocial effects are reported when RGT is undertaken compared with usual care (Weavers et al. 2014, 2016). Almost all women offered it choose to access rapid genetic counseling, and though most women undergo genetic testing eventually, only 40% opted for *rapid* access to the test. Research is needed to better understand the motivations of this test-delay group.

The present study explores the experiences of women recently diagnosed with EOC who have been offered genetic testing through the GTEOC study, and those of staff who have discussed this testing with them. We aimed to: (i) assess the impact of UGT, and (ii) integrate patients' and staff perspectives on how best to support patients, families, and professionals in developing UGT programs.

Methods

Context: The GTEOC Study

The GTEOC Study offered genetic testing to women over 18 years old diagnosed with EOC within the last 12 months through six sites in East Anglia (England). Two hundred and thirty two women were recruited between July 2013 and June 2015, irrespective of age and family history of cancer. In anticipation of the movement towards routine genetic testing for *BRCA1/BRCA2* within oncology settings, eligible women were first approached by a research nurse/trial coordinator at their treating hospital and provided with written study

information. Following this, further information was provided by the study genetic counselor (HS, who holds a Master's degree in Genetic Counseling) during a telephone call. While this would not be considered standard "comprehensive" genetic counseling, the telephone call enabled the women to raise concerns and ask any questions. The written information and that provided orally by the study genetic counselor emphasised the potential clinical impact for the women themselves and their families, as well as the contribution to research. However, the specific information provided by the local research nurses and clinical trials co-ordinators, who were briefed about the study, was not recorded. Genetic testing results were mailed to GTEOC participants and those with a mutation, variant of uncertain clinical significance (VUS) or significant family history of cancer were invited for face-to-face genetic counselling with the local Clinical Genetics department. Those with a mutation or VUS also received a follow-up telephone call from the study genetic counselor (HS). Please see Plaskocinska et al. (2016) for further details about the main GTEOC Study.

Procedure for the Qualitative Sub-study

The GTEOC Study had full ethical approval (REC12/EE/0433). Women enrolled in the GTEOC Study and who had received their *BRCA1/BRCA2* results were eligible to take part in the qualitative interviews. Purposive sampling was undertaken to ensure that participants with each outcome of genetic testing (i.e. mutation, no mutation and VUS) were recruited. Consistent with IPA methodology, the sample was selected on the basis that it could offer insights into a particular experience from the perspective of particular people (Smith et al. 2009). Fifteen women recruited earliest to the GTEOC Study (4-12 months since recruitment) received an additional telephone call from the study genetic counselor (HS) and were then provided with written information. All six staff members who had been involved in

approaching potential participants for the GTEOC Study were also invited to take part using analogous procedures. IPA studies are conducted on relatively small sample sizes as the principal concern is to provide a detailed account of individual experiences (Smith et al. 2009). Smith et al. (2009) propose that attention should be given to quality, not quantity, and given the complexity of most human phenomena, studies benefit from a concentrated focus on a small number of cases. They suggest that larger datasets can in fact inhibit the detailed case-by-case analysis that is called for.

Participants

The twelve women interviewed were broadly representative of the larger study population, with a mean participant age of 66.75 years (range 49-80). Eleven women (91.7%) were white British and eight (66%) had offspring. Ten women (83.3%) had been educated to secondary level and two (16.7%) to degree level. Two women (16.7%) had a personal history of breast cancer and both of these women were identified as having a *BRCA1/2* mutation. Altogether, these women represented the different outcomes of genetic testing (mutation (n=4), no mutation (n=5) and VUS (n=3)). Five staff members were interviewed: four of these were women, three of whom are research nurses with over 10 years' experience and one is a trial coordinator with less than 5 years of experience. One staff participant was male, a trial coordinator with over 10 years of experience. None of these staff had received any formal training in counseling around genetic testing.

Data Collection and Analytic Approach

Following written consent, semi-structured, in-depth interviews were conducted, each lasting between 25 and 90 min. Interviews explored participants' opinions and experiences of UGT, including benefits, burdens, utility of the information, and family communication. Topic guides were used, but conversations were reflexive in order to gather rich and nuanced data (Rubin and Rubin 2005). In accordance with IPA's guiding principles, semi-structured interviews enable a rich, first-person account of participants' experiences (Kvale & Brinkmann, 2009; Smith et al., 2009). Participants have the flexibility to speak freely and develop their ideas and the interviewer may probe interesting areas that arise. HS has previous experience in qualitative research and has undertaken semi-structured interviews during her post-graduate research at Master's and Doctoral levels. Interviews were transcribed *verbatim* by HS or AD* and anonymized; participants were given pseudonyms to preserve their anonymity. Transcripts were analyzed using Interpretive Phenomenological Analysis (IPA) (Smith et al. 1999), a method with three main theoretical underpinnings. Phenomenology is a philosophical approach concerned with how things appear to us in our experience (Shinebourne 2011). It is explicitly inductive, aiming to produce an account of lived experience in its own terms rather than being theory driven (Smith et al, 2009). Secondly, IPA understands this as an intrinsically interpretive endeavor, emphasizing sense-making. It engages a double hermeneutic approach, whereby the interviewer makes sense of the participants' explorations of the meanings of their personal experiences (Giddens 1987). Thus, the researcher's own conceptions and involvement in the interpretive process are intrinsic to this methodological approach. Thirdly, IPA is an idiographic approach. It is concerned with the particular, that is, how individuals make sense of their personal experiences within their specific contexts, ahead of making any more general claims. Thus, IPA is particularly suited to exploratory studies.

HS read and re-read each transcript several times, documenting emergent themes. In keeping with IPA, these were broad and descriptive themes. Theme development was iterative and reflexive, contrasting patient and staff interviews. Connections between themes were noted, themes were clustered and organized into super-ordinate concepts and then checked back against the primary data. SF and C M-S undertook independent audits of the data (SF for GTEOC participants and CM-S for staff) to independently verify and validate the themes. NH-W also independently analyzed two transcripts as part of analytic validation. The final thematic framework was reached by consensus within this authorship sub-group.

Results

The results attend to themes relating to participants' experiences of UGT, which are grouped under two themes: *motivations and influences around offers of genetic testing* and *the impacts of genetic testing in ovarian cancer patients*. Notably, throughout all accounts a further theme was emergent: ovarian cancer as the profound intrusion, whilst the impact of genetic testing was often minimized. This finding is an important contextualization for this paper.

Theme 1: Motivations and Influences around Offers of Genetic Testing

This theme highlights the contextual nature of UGT within the wider experiences of women and their families at the time of ovarian cancer diagnosis, especially considerations about genetic testing in relation to the primary concern of the cancer diagnosis itself. It is of note that staff expressed surprise at the variability of women's interest in genetic testing, as they had presumed uptake by almost all women.

Genetic Testing was Just Not Disruptive in the Context of Cancer Diagnosis

Participants suggested that undergoing genetic testing was not a substantial concern for them in the context of having been diagnosed with ovarian cancer and indeed, being confronted with their own mortality. In some cases, there were explicit comparisons between the considerably bigger impact of cancer diagnosis and treatment with other matters, such as genetic testing, which paled into insignificance as demonstrated in the interview with Glenys, when asked about when she was offered genetic testing:

Glenys: *I don't remember the ins and outs. I just know that they said that Dr (name removed) would like to see me.*

Interviewer: *Yeah. To discuss it.*

Glenys: *That was all. Yeah.*

Interviewer: *Yeah.*

Glenys: *I mean I was going- I was going through chemo at the time an, you know, I just wanted to get through the chemo (laughing tone) I really didn't really care about- you know, as long as I was gonna be all right, that was all I was concerned about.*

Interviewer: *Yeah, yeah.*

Glenys: *And that's made a big difference to my attitude to all the tests and studies and everything.*

Interviewer: *Yeah.*

Glenys: *Because I knew that once, you know, the op had been done, that I was ok. And every time I had a test, a scan or whatever, I was told that I was in the clear.*

Interviewer: *Yeah.*

Glenys: *That made a huge difference to my attitude, you know.*

(Glenys, 55 years old, no BRCA1/2 mutation identified, mutation identified in another inherited cancer gene)

Glenys foregrounds her treatment, explaining that as her primary concern ahead of anything else. In other interviews, the contrast is more implicit. Unlike the women's accounts of cancer diagnosis and treatment, in which there are spontaneously given, long descriptions of specific events and the derailing impact on the women's lives, the accounts about genetic testing tended to be minimal, despite interviewer prompting for further detail. Indeed, in several cases, participants could not recount when they were initially offered genetic testing and explained that such offers were not problematic. Consider the two extracts below, taken from the interview with Sandra, a 68-year-old woman who had a *BRCA1/2* mutation identified. Earlier in the interview she had discussed her previous diagnosis of breast cancer as well as her strong family history of cancer, including both of her parents and more distant relatives. First is an extract in which she explores the dramatic and disruptive events of her diagnosis of ovarian cancer and the lead up to it. At the time, she was also the primary carer for her husband, who had a chronic health condition:

Sandra: *By then, I'd stopped eating because I was getting my husband a meal but having to keep popping outside for fresh air while I was even cooking his meal. And I thought, "I can't go on like this." And I'd lost- For about a*

month they did that. All of June. And then by July I'd lost- I lost four stone in about three weeks.

Interviewer: *Yeah. Wow.*

Sandra: *And I had very very little energy and I was beginning to get really worried, not for myself but for my husband cos I couldn't- I was getting to feel I couldn't look after him. And I went to see the doctor and I hadn't seen her for nearly two months and she said, "You've lost a lot of weight," and I said, "Yeah, I'm not feeling at all well." And I said, "I keep having- The doctor said last week he'd send the nurse in" I said "and she did me three suppositories and I had to drink five drinks straight away" I said "and I still didn't go." So she rang the hospital and they said "Come in immediately".*

Interviewer: *Yeah*

Sandra: *I came home and sorted pills and things for my husband, got myself ready, went in and of course by midnight they'd done X-rays and I knew I hadn't got a bowel blockage that was on the Tuesday night. Thursday morning- By Thursday I'd had scans and I'd had all sorts of things and tests, and you name it I'd had it. And that's when Dr (name removed) came and said "We think you have secondary breast cancer". Cos all here swelled up as well. I couldn't bend at all. All here was tight and she said it was something to do with the lymph nodes but I can't remember what it was. And she said, "You have secondary breast cancer and we're ninety-nine and three-quarter percent sure that you have ovarian cancer and we think it's Stage 4."*

Interviewer: *Wow.*

Sandra: *Well I didn't know what that meant and I said "Oh ok. What do we do now?" and she sent this little Macmillan nurse to talk to me but I couldn't cope with her. (laughs) She was sweet but she was too sweet!*

Interviewer: *Right. Just not appropriate at that time for you at all.*

Sandra: *No (laughs). I didn't need sweetness and condescension and I don't mean that in a nasty way. She was a lovely lady and she was trying her best and probably for another type of character, she would've been right. They could've sat and held hands and the patient could've cried and- but it annoyed me, I didn't need it. I didn't want it. I just wanted to process everything in my own mind and decide how I felt and what was going to happen. And about five minutes after the doctor had gone and she'd gone, I asked her to go erm it suddenly hit me then and I just thought I'm in a room full of people so I just took myself-*

Interviewer: *You were you on a ward were you?*

Sandra: *Yeah, I was on the ward, yeah. And erm I just took myself off into the loo, sat on the floor, had a good cry and thought, "Right, you've got it out of your system, let's get started."*

In contrast with the physical, emotional and logistical impacts surrounding her cancer diagnosis, Sandra had little to say about her experience of genetic testing, which was described as unproblematic:

Interviewer: *Do you have any kind of comments or feedback about going through that genetic testing? I mean I know we spoke, so once you'd said you were*

interested, you were put in touch with me. Was that ok having that done by phone?

Sandra: *Yeah, it wasn't a problem to me.*

Interviewer: *Yeah ok, that's good*

Sandra: *I didn't find it difficult or upsetting or anything.*

Interviewer: *Was there enough information and so on for you?*

Sandra: *Oh yes yes.*

Interviewer: *Yeah and I mean obviously, you were given a positive result-*

Sandra: *I think anyone with a normal intelligence could understand it easily.*

Interviewer: *Good.*

Sandra: *Yeah I didn't find it a problem at all.*

Interviewer: *Yeah and you felt you could get any questions answered that you wanted to?*

Sandra: *Yes, yes, yes and I felt it was a good thing to do and I think if everybody did it when they were asked, then it all helps with knowledge and future information.*

Women valued the minimal logistical impact incurred by having genetic testing through the study, though again this may be a comparison with the direct disruption of cancer. Joy, a 49 year old, who had no *BRCA1/2* mutation identified discusses the minimal disruption (and impact to her) of genetic testing:

Interviewer: *So, did you have any concerns and anxieties?*

Joy: *No, because it's very- it's not invasive, it's not- did- It was just filling in forms. It wasn't like I had to go and have a surgical procedure for it or anything like that. Or take some medicine for it or anything….I wasn't relieved because it didn't really matter to me because I still had ovarian cancer, you know. It wasn't a positive or a negative for me but- I did tell my sister straight away, so she could put her daughter out of her misery.*

Social Altruism and Family Considerations were Highly Persuasive

Two main social influences were discussed by participants as impacting UGT uptake decisions: *altruism and family involvement*. This covers both how the women considered others in their decision-making process, and also how others are reported to have actively influenced that choice. Every participant made reference to *altruism* as a motivation for them to have genetic testing. Primarily this was oriented towards their family, in particular their daughters, although other female relatives were also discussed, as demonstrated by Justine, a 71-year-old in whom no *BRCA1/2* mutation was identified:

Interviewer: *So, do you remember who first mentioned that to you?*

Justine: *Yes. It was now- it was either the chemo doctor or it was the surgeon, one or the other said that I'd be- And I said, 'Of course'. Obviously, because I've got a niece, and obviously, I needed to know for her.*

Interviewer: *You have a sister- is it sister? a brother?*

Justine: *I've got two brothers, yeah. But- And I'm quite happy to sort of take part in things, if it helps other people, obviously. I mean, it's not just me, is it? I'm just sort of one. Yeah.*

Interviewer: *So, in general you're quite happy to take part and so on.*

Justine: *[Yes, yes]. Oh, yes. Of course.*

Interviewer: *So, this wasn't something that it was a big decision to make in your mind then?*

Justine: *No, no, no.*

In many cases this further extended to unrelated others, as exemplified by the interview with Joy (no *BRCA1/2* mutation identified):

Interviewer: *The genetic testing as well, do you think it was um an appropriate time to be approached about it?*

Joy: *I don't think that it would've mattered when you approached me to be honest, at the time I was probably not very with it to be perfectly blunt.*

Interviewer: *Yeah.*

Joy: *But if it needed to be done then then it needed to be done then. It didn't upset me.*

Interviewer: *Yeah, Ok.*

Joy: *And it didn't cause me a problem.*

Interviewer: *And it's probably not something that you were overly concerned about-?*

Joy: *No.*

Interviewer: *Thinking it was relevant to you, which in the end it didn't turn out to be?*

Joy: *No. I didn't think it was relevant to me. But I thought if I could help- if it would help diagnose somebody earlier in the future, then it's worth doing.*

Here Joy backgrounds the significance of genetic testing at the time it was offered, due to her health status at the time. Nevertheless, she demonstrates that she had a willingness to go ahead with it. The interviewer then draws upon a comment Joy had made earlier in the interview about the limited relevance of genetic testing to herself and her family, primarily because she does not have children. Joy then draws upon the notion of future oriented altruism towards other women at risk of ovarian cancer.

All staff participants indicated altruism was the primary motivation of participants, as demonstrated by the following extract involving Stephen, a clinical trials coordinator:

Interviewer: *It'd be good to hear your opinions on the sort of pros and cons of offering genetic testing to people quite soon after they're diagnosed.*

Stephen: *I guess the pros are that most patients, you know, when you speak to them are very keen to know why they've got cancer. Most people you speak to, they want to know why, what the impacts are for their families, children, siblings and so on.*

Interviewer: *Yeah.*

Stephen: *I don't see any real disadvantages.*

Beyond the internal motivations of individual participants, *family involvement* emerged as a more extended component of this theme. Some women discussed their interactions with relatives, noting their interest or otherwise in genetic testing. This impacted upon the women's decision making about UGT, as discussed by Lynn (no *BRCA1/2* mutation identified):

Lynn: *Jessica (daughter) never says much but our Laura (daughter) said, "Mum is it like contagious or can we get it?"*

Interviewer: *Yeah, yeah.*

Lynn: *You know, does that mean because you've got it are we going to get it?*

Interviewer: *Yeah, yeah.*

Lynn: *Jessica (daughter) tends to be quieter about things.*

Interviewer: *But it's a question that comes to mind?*

Lynn: *But it's a question that comes to mind. And you know, she's asked since. And that's why we did- agreed to the genetics. We said, "Why not", you know. We were tested- many years ago they looked into the genetics of the girls because Laura (daughter) was born with half her waterworks missing.*

Sometimes family involvement complicated decision making and led to ambivalence in the women:

"When I got the [invitation to GTEOC] letter, I spoke to [sister] about it, and [sister] thought, "No, you're doing enough already". And then I was thinking, "Oh should I go through with it or not?"" (Rita, VUS identified in BRCA1/2)

Though Rita had expressed that she would like to pursue genetic testing, she now felt conflicted in her decision making, between her own desire on the one hand and her responsibilities towards her sister and other relatives on the other. Furthermore, staff gave examples of family members, particularly offspring, swaying a woman's decision to participate or not, because of the impact on themselves:

"I had one where there were two daughters. One daughter was quite happy, the other daughter wasn't, she didn't want to know and- I said, "Well it's got to be something you all discuss as a family really and decide what's best for you at this point in time."…And they did and decided not to go into the trial. So you know, that's what it's gotta be, hasn't it?" (Research Nurse, Sally)

Here we see an account of complex negotiations. Firstly, the woman offered UGT must consider her own desires and anticipate those of her offspring. This can be complicated further by division within the family unit. Secondly, we have some insight into how Sally negotiates her active and dynamic role in managing this situation as she seeks to facilitate discussion and agreement within the family.

Staff Anxieties Regarding Additive Emotional Burden to some Already Vulnerable Patients

Unlike the women's accounts, staff did not minimize the psychological effects of offering UGT so soon after a diagnosis of ovarian cancer. Rather, they told accounts of thoughtful

consideration of the best time to approach women on this subject. This is intricately related to the context of their experiences of ovarian cancer diagnosis as burdensome and overwhelming. This theme speaks powerfully of the group which are so difficult to access directly - those women who decline UGT. In some cases, fear is the reason why women decline UGT, as Margaret, a research nurse explains:

Interviewer: *You mentioned that most people have been really positive about it [UGT]. For those that haven't, or have- can you just sort of expand that a bit more about sort of what has gone on for them?*

Margaret: *Very few that haven't. One has just been, "I really don't want to know. It just scares me and it's not something I'll ever want to look into." But the only other couple have been if they just haven't got any family at all, they don't know their family history. They're either adop- we had one who's adopted, one who's had no children and just it's very much the minority.*

Interviewer: *Yeah.*

Margaret: *I mean every patient virtually I've spoken to will have wanted to certainly go ahead onto the conversation with yourself.*

Another aspect to this theme is the pre-existing emotions the women experience due to their recent ovarian cancer diagnoses:

"Once they've had a diagnosis they're bamboozled with the idea of all the treatment options in front of them or they might be post-surgical and facing chemo…and- they're probably not at the most receptive point to consider this. They're already on this sort of rollercoaster, they're in shock." (Research nurse, Fiona)

Fiona highlights the emotional burden of the cancer diagnosis and all it entails as directly impacting on women's desire and capacity to contemplate decisions about UGT. Her use of emotive words builds a picture of someone who is not emotionally available for further discussions. Furthermore, staff participants related psychosocial concerns as pertinent to their gatekeeping role when deciding whether to approach women or not, as discussed by Chloe, a clinical trials coordinator:

Chloe: *Certainly, other people I've spoken to so far have been happy to be approached about it and I think they in general seem to think it's a good thing, even if they have their own personal reasons for not wanting to do it themselves.*

Interviewer: *Ok. Yeah. So, as in they're happy that they were approached even if they're saying no?*

Chloe: *I don't know about any risks, I guess- Obviously, it's a difficult time for people so you have to be careful, but if we felt it wasn't the right time to ask people, we'd always do what we felt was right.*

Interviewer: *Yeah. So, when you say the clinicians normally approach these patients, is it usually the oncologist or um nurse?*

Chloe: *It depends on where they're seen first, really. I think (nurse's name) like me would maybe talk to patients but in a clinic setting with the surgeons.*

Interviewer: *Yeah.*

Chloe: *And again, I don't think we [pause] certainly when I do it, I don't go into too much detail, cos given that they're in quite an early stage in their diagnosis*

and there's a lot going on, I'll make them aware that there's a genetics test, a genetic study on offer that they may want to consider

Interviewer: *Yeah.*

Chloe: *And if they're happy to get some more information, I usually leave them with the info sheet and obviously say, if they have any questions.*

Theme 2: Impacts of Genetic Testing in Ovarian Cancer Patients

This theme considers the effects of the different genetic testing results on the participants and how they relate to their wider families. In particular, women have to negotiate risks to themselves and others once they receive their results.

Negative Test Results Were a Reassuring Process for Most Participants

If no mutation was detected, generally participants described feelings of reassurance and relief. They discuss little further impact, other than the knock-on effect of reassurance for their relatives, as demonstrated by Kate (no *BRCA 1/2* mutation identified):

Interviewer: *So when we sent this letter, was it ok to receive the results by a letter?*

Kate: *Absolutely fine. Yes. No problem. No. And it was quite early on as well. It was the- February? Yes, 5th of February, so it was quite-*

Interviewer: *Did it come through a bit quicker than-*

Kate: *early on with my- I was sort of barely- I'd only started chemo two or three weeks so yes it was good to receive it.*

Interviewer: *What did you think then when you did get it?*

Kate: *I was quite happy with it.*

Interviewer: *Yeah?*

Kate: *Yes. Yes.*

Interviewer: *Did it make you feel reassured about-?*

Kate: *I think that I was reassured, yes. Definitely. Yes. It meant I could tell my sister and my daughter. Yeah, in fact I must tell my sons then if it's connected with the prostate as well.*

Yes, I told her [daughter] the result. Yeah and she was, you know, happy about it. (Clare, no BRCA1/2 mutation identified)

The accounts are minimal in detail – once given the reassurance, there was little other psychological impact. Some participants explained that they interpreted a negative result within the context of their family history of cancer. For example, women with minimal family history now feel that their own diagnosis was *"just one of those things" (Joy, no BRCA1/2 mutation identified)* and that the risk to relatives is minimal. Only one patient not found to have a *BRCA1/2* mutation, Christine, continued to believe there was an undiscovered underlying genetic risk. Christine was the only patient without a *BRCA1/2* mutation with a strong family history of cancer which included her mother, father and paternal grandfather:

Interviewer: *Would it have surprised you if it [genetic test] had come back positive?*

Christine: *What that it was-*

Interviewer: *I mean if we found a gene?*

Christine: *That was possibly from my mother you mean or my father?*

Interviewer: *Yeah.*

Christine: *No, I'm pretty sure it was.*

Interviewer: *Yeah ok so you're still fairly sure that there's an inherited link.*

Christine: *Yes, because my grandfather died I think of cancer. I got his birth certificate in there.*

Interviewer: *Ok.*

Christine: *I think my other grandfather died of it as well and my grandmother, well you didn't call it cancer then, did you? I mean she died when my Mum was only about early twenties.*

Interviewer: *Oh really? Young.*

Christine: *Yeah.*

Interviewer: *Possibly of cancer again. Erm so even though we haven't found a change in these genes, you're still fairly confident there's something going on in your family?*

Christine: *Yeah.*

Interviewer: *So it wouldn't surprise you if later down the line we found something else?*

Christine: *No, no, it wouldn't surprise me.*

Interviewer: *Ok. So in a sense does the fact that we didn't find a change in the BRCA1 or BRCA2 genes, does that not put your mind at rest or make you think any different?*

Christine: *I just don't think about it really.*

Interviewer: *No.*

Christine: *No, I just- I do think probably I inherited it from my mother but as she had breast cancer. But erm and she had a hysterectomy as well.*

Trading Uncertainties: Managing a Finding of a Genetic Variant or Mutation

This subtheme relates to the complex risk management that some women must undertake once they have received a test result indicating a mutation or VUS. In the case of a mutation being detected, this provides women with an explanation for their cancer, but it brings challenges in dealing with more quantified risks to themselves and their family, which are less certain outcomes. Women with a VUS (inconclusive) result are left with even higher levels of uncertainty, like Rita:

Interviewer: *How's that for you, having that uncertainty?*

Rita: *It's a bit off, really.*

Interviewer: *Yeah.*

Rita: *Because I was thinking, well, she- coming to see her and she can definitely give me an answer but she can't because they're not quite sure of one of the genes. She says whatever every- all of us have different genes, you know,*

abnormal genes and things like that so she can't give them a straight answer to say- about these genes. Or they have to test them to find out.

Interviewer: *Yeah. Did she say what the plan is? Is there a plan?*

Rita: *No, there isn't a plan, she just said to my doctor that within three years' time they might get to know more about this gene and they can phone up and find out*

Interviewer: *If there's some more knowledge*

Rita: *[Yes], and more knowledge about it. But for now they're not certain what it is*

Janette discussed the uncertainty that remains for her, despite her conclusive genetic test result. Janette was diagnosed with breast cancer thirty-five years ago (at age 28 years), and has remained well until now. She still has one breast and discusses the challenges of decision making in the face of uncertainty:

"They spoke to me, they said, you know, "it's an eighty-five percent chance that you will get breast cancer again or even another type of cancer", but the BRCA gene apparently reduces risk as you get older, but as you get older but the age er is more you know as you get older you have more chance of breast cancer. So, I feel I'm really- You don't know where those two meet so I just feel as though again I'm back to square one, where who knows?" (Janette, BRCA1/2 mutation identified)

Here Janette grapples with knowledge about the lifetime- and age-related breast cancer risks of someone with a *BRCA1/2* mutation and what she should choose to do about her increased risk.

Managing Responsibilities in the Wake of Genetic Testing

Receiving the results of UGT leads to responsibilities to others which must be managed by the women; in particular, negotiating family communication about the test result. Mary demonstrates the prominent concept of 'transferred responsibility'; that is, the importance of imparting the relevant information to a family member, and then foregrounding that person's autonomy in how they choose to respond to the information:

"My son's gonna contact him (other son) and go and tell him, yeah. And then it's his choice. I think, I feel that he ought to know, but whether he takes it up or not, it is down to him. He can't turn round later on and say, "Well you never told me" or something like that but- Cos he's got a daughter and two boys." (Mary, BRCA1/2 mutation identified)

Participants described many instances where these responsibilities were discharged without concern and the information was welcomed by others. However, where there are already fractious relationships or where relatives expressed lack of interest in genetic testing, communication can be problematic. The situation can become more complicated when the responsibility of providing genetic information comes into conflict with other perceived responsibilities, such as avoiding unwanted intrusion in the lives of others:

"A lot of this family I've had no contact with for many years and then I kept reading this letter and I thought you know if I got this letter from somebody … I think I might be angry too, or you know, why would you wanna tell me this when I'm happy in my life and I just feel it's a big intrusion, personally." (Janette, BRCA1/2 mutation identified)

Discussion

These findings confirm the quantitative results of the GTEOC study (Plaskocinska et al. 2016): where UGT for *BRCA1/BRCA2* is taken up, it is considered very acceptable. This finding is also reported by previous studies (Augestad et al. 2017; Meiser et al. 2012; Schlich-Bakker et al. 2006, 2008; 2009; Weavers et al. 2014, 2016; Zilliacus et al. 2012). No mutations or VUS will be identified in most women, and according to our analysis women are likely to find this reassuring. However, some of this reassurance will be false as a small proportion of women will have a mutation in *BRCA1/2* that has not been identified due to technical limitations and others will have a mutation in another ovarian cancer predisposition gene not tested for, or as yet undiscovered. We suggest that an important factor in the acceptability of UGT is the ease with which genetic testing can take place, without creating additional burdens.

Practice Implications

Our analysis has gone beyond most previous studies by demonstrating that individuals consistently position UGT within the wider context of a recent diagnosis of EOC and treatment, which are already burdensome. We suggest that this is generally in one of two ways:

1. Women (and/or their families) are willing to undergo UGT, but have limited scope for attending to the issues at present due to their cancer diagnosis
2. Women (and/or their families) are distressed or anxious when faced with UGT and experience contemplating it as *additionally* burdensome

The former raises interesting issues for discussion about informed consent and the timing of genetic testing, particularly given that in their retrospective accounts a number of women in this study could not remember discussions about UGT. Furthermore, it highlights the importance of involving knowledgeable health professionals in order to explore what many, from our analysis, experience as confusing uncertainty. The latter may shed some light on the limited uptake of genetic testing soon after cancer diagnoses reported to date (Schlich-Bakker et al. 2008). It is important that these concerns and needs are addressed, particularly as genetic testing is increasingly becoming part of routine medical care. This finding highlights the need for a continued individualized approach in clinical practice, with support and space for discussion available if desired (Foster et al. 2006). In the fast-paced medical world with increasing treatment options it can be forgotten that some individuals choose to forego genetic testing. Anxiety is prevalent in newly diagnosed cancer patients and needs to be addressed sensitively (Watts et al. 2015).

Another contribution of this study is knowledge about the broader social and familial context in relation to UGT decision making, which very much reflect consistent findings across the broader genetic counseling literature. Our participants reported both the influence of responsibility or altruism towards others in decision making and also the direct impact that other people have in influencing that very same decision. We do well to remember that people do not make decisions in isolation (D'Agincourt-Canning 2006; Hallowell et al. 2003). Indeed, Hallowell et al. (2003) describe how women depict themselves as 'selves in relation'; in generating and disclosing genetic information about themselves and their families, participants were motivated by their responsibility to further the autonomy of their relatives. D'Agincourt-Canning (2006) similarly reports participants' orientation to both their families and to unknown others in their decisions about genetic testing. This responsibility

framing bears little resemblance to theories of rational decision making, which solely focus on the individual and their autonomous decision (Faden and Beauchamp 1986). As UGT programs are rolled out, staff must continue to relate to individuals within their family contexts.

Though in most instances communication with relatives about genetic testing results is described as unproblematic, some participants discussed challenges or barriers. As genetic testing becomes more widespread, this important outcome must not be side-lined or underestimated. Women may require additional support in disseminating information and this can be experienced as burdensome (Hallowell et al. 2003). We suggest staff actively discuss the practical aspects of information dissemination with women undergoing UGT and provide written supportive materials. The identification of a key relative who can advocate on their behalf within the family may be helpful.

Study Limitations

This study has limitations, many of which are common to qualitative work. Consistent with IPA methodological guidance (Pietkiewicz and Smith 2012) we included a relatively small number of participants; it is difficult to know whether their experiences and perspectives are representative of the broader population that we are interested in, though ascertaining this was not the aim of the research presented here. Given the knowledge of differences in psychosocial aspects of cancer between differing ethnic groups (Alcalá 2014), the cultural homogeneity of our sample was disappointing. Furthermore, we have not had direct access to individuals who declined consent to participate in the GTEOC Study. The interviews were undertaken between 4-12 months following receipt of genetic testing results and this introduces variability that could affect women's responses. Additionally, only one interview

was undertaken with each woman and it is not known whether responses might be different at other time points.

A further potential limitation of the study is that the study genetic counselor and interviewer were one and the same person. Though this strengthens the work in some ways, for example there was already rapport with the participants, it brings risks in other aspects. For example, although some critique of the GTEOC study was presented during interviews, it may be that the participants did not feel fully able to discuss all negative aspects of the GTEOC Study. Also, despite seeking to be led by the literature and the participants themselves, it is possible that, during interviews and analysis, HS was led by some of her preconceptions and prior knowledge from earlier in the program of work, though this would have been mitigated by the involvement of the rest of the research team during analysis.

Research Recommendations

Due to difficulties of access, current research into genetic testing shortly after diagnosis has focused on those who have given consent, rather than those who have declined. Given that a significant minority may decline genetic testing (Schlich-Bakker et al. 2008), research into the experiences of these people and how best to offer testing to them is important. As UGT programs are rolled out in a variety of cancer contexts and increasingly in the context of other diseases, it is vital that the experiences of more diverse ethnic and cultural groups are included in research, in order to direct guideline development appropriately. Furthermore, research into other cancer and disease contexts where UGT is emerging and also longitudinal studies of experiences over time would be of benefit as genetic testing is increasingly applied in mainstream medicine.

Conclusion

This study has highlighted important and pertinent issues, in particular, going beyond the specific situation of UGT to considering the broader context of women's lives. Our findings have practical implications for developing contexts of UGT. The importance of the family in discussions and sensitive consideration of the timing of offers of genetic testing are highlighted. Furthermore, we emphasize the role of the clinical genetics team in providing support for staff rolling out UGT and for individuals receiving a genetic diagnosis and their families, and offer recommendations for future research.

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Compliance with Ethical Standards

Conflict of Interest Hannah Shipman, Samantha Flynn, Carey F MacDonald-Smith, James Brenton, Robin Crawford, Marc Tischkowitz and Nicholas J Hulbert-Williams declare that they have no conflict of interest.

Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

Animal Studies No animal studies were carried out by the authors for this article.

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